General

Guideline Title

Management of febrile neutropenia in adult cancer patients.

Bibliographic Source(s)

Alberta Provincial Tumour Teams. Management of febrile neutropenia in adult cancer patients. Edmonton (Alberta): CancerControl Alberta; 2014 Jan. 19 p. (Clinical practice guideline; no. SUPP-004). [54 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Alberta Provincial Tumour Teams. Management of febrile neutropenia in adult cancer patients. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Jan. 16 p. (Clinical practice guideline; no. SUPP-002).

Recommendations

Major Recommendations

Summary of Key Points

1. Febrile neutropenia is defined as:
    - Fever higher than 38.3°C OR higher than 38.0°C for more than 1 hour, in a patient who has received chemotherapy in the past month, AND
    - Neutrophils less than 0.5 x 10^9 cells/L
2. Patients suspected of having febrile neutropenia should undergo:
    - History and physical exam to determine the site of infection
    - Complete hematological profile and chemistry profile
    - Chest-x-ray
3. The preferred initial antibiotic therapy is intravenous (IV) piperacillin-tazobactam 4.5 grams every 8 hours, plus IV fluids. Cefepime monotherapy is an alternative to piperacillin-tazobactam.
4. Patients with febrile neutropenia who are felt to be at low risk of complications may be managed as an outpatient (see Table 2 in the original guideline document for characteristics of patients at low risk for complications and high risk for complications from febrile neutropenia).

Important Contact Information

After assessing the patient, call the responsible medical oncologist or the after-hours medical oncologist on-call for a consultation. The original

guideline document includes additional details and local contact information.

If septic shock is a concern, physicians and health-care providers practicing in Alberta can call the Referral, Access, Advice, Placement, Information and Destination (RAAPID) line.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Febrile neutropenia
- Cancer

Guideline Category

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Hematology

Infectious Diseases

Internal Medicine

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide clinicians (i.e., emergency room physicians and nurses) and family physicians with strategies for the management of adult patients with solid tumours or hematologic malignancies who present with febrile neutropenia

Target Population

Adult outpatients who have been treated with chemotherapy for solid tumours or hematologic malignancies within the past month and who present with febrile neutropenia

Note: Different principles may apply to inpatients and to pediatric patients.

Interventions and Practices Considered

1. Contacting on-call medical oncologist or responsible medical oncologist when any patient presents with febrile neutropenia
2. History and detailed clinical examination
3. Complete hematological profile and chemistry profile
4. Chest x-ray and other imaging as indicated by clinical picture
5. Antibiotic therapy (combination therapy, monotherapy, empiric vancomycin)
6. Outpatient management
7. Management of low-risk neutropenia

Major Outcomes Considered

- Success rate of antibiotic treatment
- Survival
- Failure rate
- Mortality

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (Patient or Population, Intervention, Comparisons, Outcomes).

Guideline Questions

1. What is the definition of febrile neutropenia for adult patients with solid tumours or hematologic malignancies?
2. What are the risk factors for febrile neutropenia?
3. What pre-treatment investigations should be conducted for adult outpatients suspected of having febrile neutropenia?
4. What antibiotic therapy regimens are recommended for the treatment of febrile neutropenia in adult patients with solid tumours or hematologic malignancies?
5. What are the recommended management strategies for adult patients with low-risk febrile neutropenia?

Search Strategy

For the January 2014 guideline update, medical journal articles were searched using Medline (1985 to September Week 1, 2013), EMBASE (1985 to November Week 1, 2013), Cochrane Database of Systematic Reviews (1985 to 3rd Quarter, 2013), and PubMed electronic

databases; the references and bibliographies of articles identified through these searches were scanned for additional sources.

The search terms included: Neutropenia [MeSH term] AND Fever [MeSH term], AND Neoplasms [MeSH term] OR Lymphoma [MeSH term], AND Drug Therapy [MeSH term] OR Drug Therapy Combination [MeSH term], AND clinical trial OR controlled clinical trial OR meta analysis OR multicenter study OR practice guideline OR randomized controlled trial.

Articles were excluded from the final review if they: had a non-English abstract, involved only pediatric patients, or were published prior to January 1985. A systematic search for new or updated practice guidelines published since January 2010 was also conducted. Guidelines from the National Comprehensive Cancer Network (NCCN), British Columbia Cancer Agency (BCCA), and Infectious Diseases Society of America (IDSA) were deemed to be most relevant and corresponded best with local context and practice.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

For the development of the original guideline, evidence was selected, reviewed, and endorsed by a working group comprised of oncologists specializing in breast, ovarian, colorectal, and lung cancers, hematologists, and family physicians, as well as two Knowledge Management Specialists from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic will be assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

In order to achieve consensus on the key points in the original guideline document, a survey based on the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument was sent to oncologists, hematologists, infectious diseases specialists, and family physicians. The survey contained items that asked reviewers to rate their level agreement with each of the key points, as well as their level of agreement that the key points were evidence-based. Other survey items included level of agreement that the guideline questions, search strategy, and target audience were each clearly described, overall agreement with the guideline, and willingness to recommend use of the guideline. For all items, a 7-point scale, ranging from strongly agree (7) to strongly disagree (1), was used. Respondents were also permitted to provide open-ended comments on each item. A total of 8 reviewers responded with feedback. There were five medical oncologists, one family physician, one infectious diseases specialist, and one general internist working mainly in oncology, representing Calgary, Edmonton, Red Deer, Grande Prairie, and Medicine Hat. Survey items that achieved a score of 6 to 7 from at least 80% of the reviewers were deemed acceptable without further edits; all other survey items were deemed important areas for consideration and/or revision.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The original version of this guideline was created and reviewed by the Alberta Medical Affairs and Community Oncology (MACO) Medical Liaison Team in November 2008; the guideline was updated and approved by the MACO team in January 2012 and was reviewed and approved by members of the CancerControl Alberta Medical Liaison Committee in January 2014.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management (KM) Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of febrile neutropenia in adult cancer patients

Potential Harms

In one randomized trial, imipenem therapy was associated with significantly greater toxicity than ceftazidime therapy, requiring discontinuation in 10% of recipients.

Qualifying Statements

Qualifying Statements

- The recommendations contained in this guideline are a consensus of the Alberta Provincial Tumour Teams and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.
- These guidelines are for the management of adult cancer patients with febrile neutropenia. Every patient has a unique presentation and should be managed as such. Daily reassessments are required to ensure that the patient is recovering satisfactorily.

Implementation of the Guideline

Description of Implementation Strategy

- Post the guideline on the Alberta Health Services website.
- Circulate an electronic version of the guideline to members of the Alberta Provincial Tumour Teams.
- Include a link to document in other relevant clinical practice guidelines on the Alberta Health Services Web site.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Jan (revised 2014 Jan)

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

There was no direct industry involvement in the development or dissemination of this guideline.

Guideline Committee

Alberta Provincial Tumour Teams

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

Participation of the working group members in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. While some members of the working group are involved in research funded by industry or have other such potential conflicts of interest, the developers of this guideline are satisfied it was developed in an unbiased manner.

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This guideline updates a previous version: Alberta Provincial Tumour Teams. Management of febrile neutropenia in adult cancer patients. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Jan. 16 p. (Clinical practice guideline; no. SUPP-002).

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 13, 2012. The information was verified by the guideline developer on February 1, 2013. This summary was updated by ECRI Institute on April 28, 2014. The updated information was verified by the guideline developer on May 23, 2014.

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